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Allergic diseases and novel targets in allergen immunotherapy

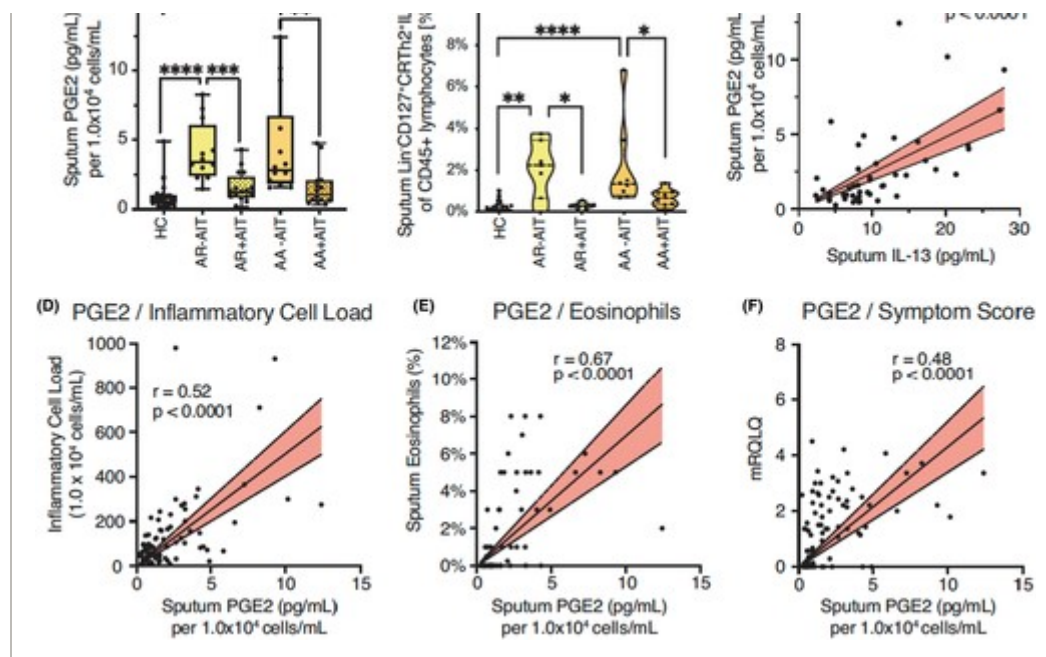
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Allergic asthma (AA) is heterogeneous in both its clinical profile (phenotype) and the mechanisms underlying it (endotype).^{1, 2} Eosinophilic or type-2 asthma is associated with the elevation of pro-inflammatory mediators, which can also be evident in the airways of allergic rhinitis patients without asthma. This raises the concept of ‘united airways’, which postulates that upper and lower airways are morphologically and functionally singular and display homogeneity in physical barrier maintenance, immune responses and mucociliary clearance. Consequently, sputum, containing cells and other components of the central airway, can inform an understanding of processes occurring lower in the airways. Production of type-2 inflammation-promoting mediators, such as PGE2 and IL-4, was shown to be mediated by microRNAs (miRs) – small molecules with the capacity to post-transcriptionally regulate gene expression, highlighting their relevance in allergic inflammation. Moreover, epithelial miR-218-5p was also reported to confer a protective role in eosinophilic airway inflammation.³ Little is known of how allergen-specific immunotherapy (AIT) affects local miRs and levels of corresponding gene transcripts of asthma patients. The study conducted by Jakwerth et al.⁴ identified miR-3935 as one of the most relevant out of four miRs up-regulated in asthmatics undergoing AIT, as its target PTGER3, the prostaglandin EP3 receptor, was down-regulated compared to untreated asthmatics. Subsequently, sputum supernatants obtained from asthmatics contained elevated levels of its ligand PGE2 and ILC2 numbers compared to the AIT-treated group. Importantly, sputum PGE2 levels correlated with numerous markers of allergic inflammation: IL-13 levels, inflammatory cell load, eosinophil count and clinical symptoms score (Figure 1). Altogether, the results of this study provide evidence of AIT-related epigenetic regulation in the airways of AA patients and present a potential candidate to be researched in future studies to determine its value as a treatment efficacy marker.



**FIGURE 1**[Open in figure viewer](#) | [Download PowerPoint](#)Is derived from ref⁴

Allergic rhinitis and asthma are prevalent respiratory pathologies, most commonly triggered by such aeroallergens as dust mites, animal dander, fungal spores and pollen grains.⁵ Among the latter, particularly little is known about molecular and immunological properties of poplar (*Populus nigra*)-derived pollen extract, even though it triggers allergies in up to 30% of the population within the United States, Iran, United Arab Emirates, Turkey and Hungarian, and Eastern provinces of Saudi Arabia. Notably, identifying pro-allergenic compounds within the pollen grain is fundamental for the successful design of allergen-specific immunotherapies and the diagnostics of the condition. To address this gap, Shams et al.⁶ generated a highly purified poplar pollen extract, proteins of which were separated using SDS-PAGE. Then, sera of 20 *P. nigra* sensitized individuals containing *P. nigra*-specific IgE was used for immunoblotting and identification of proteins of the most remarkable reactivity; 14 kDa profilin Pop n 2 was identified. Following this, *P. nigra* pollen-derived RNA was reverse transcribed to cDNA using primers based on the profilin protein conserved sequence of the *P. nigra*-related species which was subsequently used to generate recombinant plasmid using *E. coli*. An open reading frame of 396 bp, which encodes 131 amino acid residues, was identified upon sequencing. Recombinant Pop n 2, produced by *E. coli*, was purified, and its reactivity to poplar-specific IgE was confirmed via ELISA and immunoblotting. These findings confirm the relevance of Pop n 2 as an allergen within the poplar pollen extract and can inspire the design of new treatment strategies.

Cat allergy affects at least 1 in 10 of the population in the United States, including those who live with cats.⁷ Individuals sensitized to some aeroallergens, who fail to respond to conventional symptomatic medication, may opt for allergen-specific immunotherapy (AIT),

which can confer a lasting clinical benefit by inducing blocking allergen-specific IgG and modulating T cell responses.⁸ However, the efficacy of AIT in the context of cat allergy remains inconsistent. Partial immunological tolerance can be induced by natural exposure to cats, potentially mediated by IgG; both levels and affinity are relevant factors. However, baseline clinical and immunological triggers for cat allergy need to be identified to develop successful treatment approaches. To address this, Wambre and colleagues⁹ recruited two groups of cat sensitized asthmatics living with cats (WC) and without cats (WoC), and their clinical and immunological responses were compared. Although no differences between the two groups were observed in disease manifestation profiles or levels of IgE specific to cat dander and major cat allergen Fel d 1, the WC individuals demonstrated significantly higher IgG4 levels for both of these cat allergy triggers. Interestingly, only Fel d 4-specific IgE was the more elevated in the WC group. Moreover, basophils of WC individuals were significantly less sensitive to Fel d 1 than WoC, which correlated with serum Fel d 1-specific IgG4. In cat allergic asthmatics, who live with cats, in comparison to those who do not, Th2A polarization was favoured in response to Fel d 1, which also correlated with Fel d 1 sIgE levels. Conclusively, this study does not support the induction of tolerance with natural cat exposure. However, it demonstrates that it is critical to design studies with careful consideration for patient baseline characteristics. Figure 2.

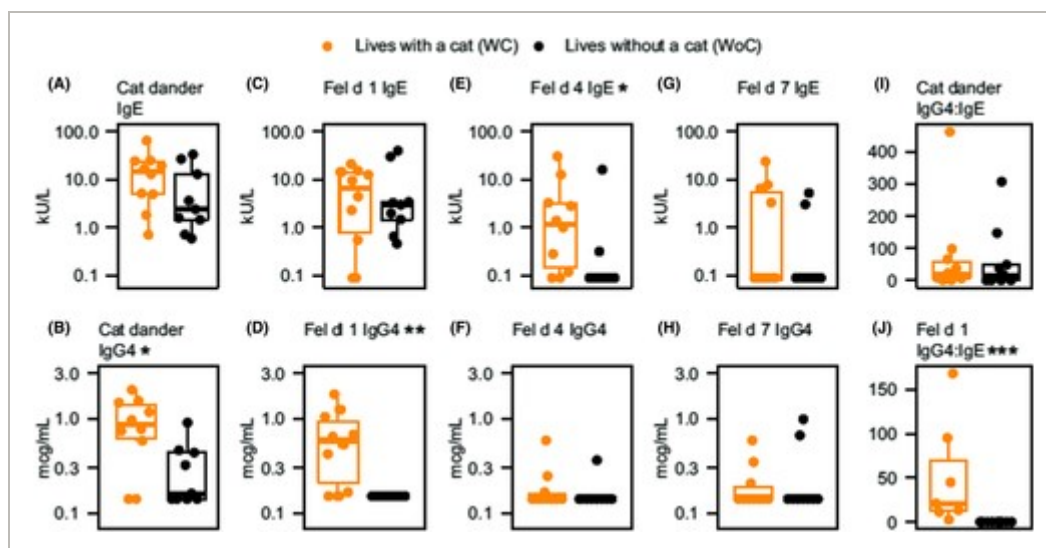


FIGURE 2

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REFERENCES

- 1 Chen M, Shepard K 2nd, Yang M, et al. Overlap of allergic, eosinophilic and type 2 inflammatory subtypes in moderate-to-severe asthma. *Clin Exp Allergy*. 2021; 51(4): 546- 555. [doi:10.1111/cea.13790](https://doi.org/10.1111/cea.13790) . Epub 2021 Jan 7. PMID: 33217063; PMCID: PMC8048421. [Wiley Online Library](#) | [CAS](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

2 Salvermoser M, Zeber K, Boeck A, Klucker E, Schaub B. Childhood asthma: Novel endotyping by cytokines, validated through sensitization profiles and clinical characteristics. *Clin Exp Allergy*. 2021; **51**(5): 654- 665. doi:10.1111/cea.13858 . Epub 2021 Mar 14 PMID: 33650157.

[Wiley Online Library](#) | [CAS](#) | [PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

3 Liang Y, Feng Y, Wu W, et al. microRNA-218-5p plays a protective role in eosinophilic airway inflammation via targeting δ -catenin, a novel catenin in asthma. *Clin Exp Allergy*. 2020; **50**(1): 29-40. doi:10.1111/cea.13498 . Epub 2019 Oct 6 PMID: 31520422.

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4 Jakwerth CA, Chaker AM, Guerth F, et al. Sputum microRNA-screening reveals Prostaglandin EP3 receptor as selective target in allergen-specific immunotherapy. *Clin Exp Allergy*. 2021. doi:10.1111/cea.14013 . Epub ahead of print. PMID: 34514658.

[Wiley Online Library](#) | [PubMed](#) | [Google Scholar](#)

5 Orban NT, Jacobson MR, Nouri-Aria KT, Durham SR, Eifan AO. Repetitive nasal allergen challenge in allergic rhinitis: priming and Th2-type inflammation but no evidence of remodelling. *Clin Exp Allergy*. 2021; **51**(2): 329- 338. doi:10.1111/cea.13775 . Epub 2020 Nov 30 PMID: 33141493.

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6 Shams MH, Assarehzadegan MA, Eskandari N, et al. Molecular and immunochemical characterization of Pop n 2: a new allergen of Populus nigra pollen. *Clin Exp Allergy*. 2020. doi:10.1111/cea.13789 . Epub ahead of print. PMID: 33210791.

[PubMed](#) | [Web of Science®](#) | [Google Scholar](#)

7 Scadding GW, Eifan A, Penagos M, et al. Local and systemic effects of cat allergen nasal provocation. *Clin Exp Allergy*. 2015; **45**(3): 613- 623. doi:10.1111/cea.12434 . PMID: 25303516; PMCID: PMC4778413.

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8 Wraith DC, Krishna MT. Peptide allergen-specific immunotherapy for allergic airway diseases- State of the art. *Clin Exp Allergy*. 2021; **51**(6): 751- 769. doi:10.1111/cea.13840 . Epub 2021 Feb 17 PMID: 33529435.

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9 Wambre ER, Farrington M, Bajzik V, et al. Clinical and immunological evaluation of cat-allergic asthmatics living with or without a cat. *Clin Exp Allergy*. 2021. doi:10.1111/cea.14024 . Epub ahead of print. PMID: 34599624.

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